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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/882,950	06/26/1997	STUART A. KAUFFMAN	2860-27	4671
23601 7590 01/10/2002 CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			EXAMINER CHAKRABARTI, ARUN K	
			ARTUNIT	PAPER NUMBER
			1655 DATE MAILED: 01/10/2003	29

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.

Applicani (s)

08/882,950

Art Unit

Kauffman



Office Action Summary Examiner Arun Chakrabarti 1655 -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ 3 ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). Status 1) Responsive to communication(s) filed on Jul 6, 2001 2b) This action is non-final. 2a) This action is FINAL. 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213. Disposition of Claims is/are pending in the application. 4) X Claim(s) 1-50 4a) Of the above, claim(s) _______is/are withdrawn from consideration. is/are allowed. 5) 🗌 Claim(s) 6) 💢 Claim(s) 1-50 is/are rejected. is/are objected to. 7) Claim(s) ______ 8) Claims ______ are subject to restriction and/or election requirement. **Application Papers** 9) \square The specification is objected to by the Examiner. 10) The drawing(s) filed on ______ is/are objected to by the Examiner. 11) The proposed drawing correction filed on ______ is: a) \square approved b) \square disapproved. 12) \square The oath or declaration is objected to by the Examiner. Priority under 35 U.S.C. § 119 13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d). a) ☐ All b) ☐ Some * c) ☐ None of: 1. \square Certified copies of the priority documents have been received. 2. \square Certified copies of the priority documents have been received in Application No. $_$ 3.
Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). *See the attached detailed Office action for a list of the certified copies not received. 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). Attachment(s) 18) Interview Summary (PTO-413) Paper No(s). 15) X Notice of References Cited (PTO-892) 19) Notice of Informal Patent Application (PTO-152) 16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s).

20) Other:

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DETAILED ACTION

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. A new office action is hereby being forwarded.

Claim Rejections - 35 USC § 112

- 2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
 - The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
- 3. Claims 13-15 and 46-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Although specification on page 24 describes a mathematical and theoretical calculation how to obtain 1 million and 100 million different enzymes, the applicant fails to show that they had possession of 10,000 to 100,000,000 different enzymes in real practice.

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Claim Rejections - 35 USC § 102

- 4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
 - (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.
- 5. Claims 1-12, 16-22 and 25-28 are rejected under 35 U.S.C. 102 (e) as being anticipated by Civelli et al. (U.S. Patent 5,441,883) (August 15, 1995).

Civelli et al teach a method for the production of an organic molecule having a desired property (Example 6), comprising the steps of :

- a) inherently providing a reaction mixture with at least 10-100 different organic molecules in solution in the same reaction container (Example 6, as obtained by denaturation of single-stranded cDNA);
- b) causing at least one chemical reaction to take place with at least some of the different organic molecules in the reaction mixture to create a reaction mixture having one or more organic molecules different from the organic molecules in the starting group of the previous step (PCR reaction products of Example 6, Column 18, lines 10-25);
- c) repeating step (b) at least once causing at least one chemical reaction to take place with at least some of the organic molecules in the reaction mixture from the previous step of repetition to thereby produce a final reaction mixture as a result of the last repetition (Example 6, Column 17, line 52 to Column 18, line 47);

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d) screening the final reaction mixture resulting from step c) for the presence of the organic molecule having the desired property (Example 6, Column 18, lines 11-47).

Civelli et al teach a method further comprising the step of isolating from the final reaction mixture the organic molecule having the desired property (Figure 8).

Civelli et al teach a method further comprising the step of determining the structure or functional properties characterizing the organic molecule having the desired property (Example 6, Column 18, lines 26-47).

Civelli et al teach a method further comprising the step of synthesizing the organic molecule having the desired property (Example 6).

Civelli et al inherently teach a method further comprising the step of adding more of the starting group of different organic molecules to the intermediate reaction mixture after at least one repetition step (b) (Example 6, Column 18, lines 11-13).

Civelli et al inherently teach a method wherein the different organic molecules of the starting group all share a common core structure (Example 6, in this case denatured cDNA products).

Civelli et al teach a method wherein the different organic molecules of the starting group is selected from nucleotides (Example 6, Column 17, lines 43-52).

Civelli et al teach a method wherein at least one chemical reaction for each repetition step is selected from addition (Example 6, polymerase chain reaction in this case).

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Civelli et al teach a method wherein the chemical reaction is caused by changing the conditions of the intermediate reaction mixture by changing temperature (Example 6, Column 18, lines 11-13).

Civelli et al teach a method wherein the at least one chemical reaction is caused by adding a set of different enzymes (Example 6, Reverse transcriptase and RNA polymerase in this case)

Civelli et al teach a method wherein the conditions causing the chemical reaction of steps b) and c) are the same (Example 6, conditions of PCR reaction in this case).

Civelli et al teach a method wherein the method further comprises the step of using a selection method on the intermediate reaction mixture to produce a subset of organic molecules with a higher likelihood of producing the organic molecule having the desired property (Figure 8 and Example 6, Column 18, lines 11-47).

Civelli et al teach a method wherein the selection method comprises using a chemostat (Example 6, a Tris-Cl buffer in this case).

Civelli et al teach a method wherein at least one agent is a reducing agent (Example 6, DTT in this case).

6. Claims 36-45 and 49-50 are rejected under 35 U.S.C. 102 (e) as being anticipated by Iacobucci et al. (U.S. Patent 5,350,681) (September 27, 1994).

Iacobucci et al teach a method for the production and generating for characterization of an organic molecule having a desired property (Abstract), comprising the steps of:

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- a) reacting a group of different enzymes representing a diversity of catalytic activities under suitable conditions with a group of different substrates to create a reaction mixture, thereby producing one or more organic molecules different from the enzymes and substrates in the reaction mixture (Abstract and Example 11-12 and Figures 2 and 9);
- b) screening the reaction mixture for the presence of the organic molecule having the desired property (Abstract and Examples 11-12 and Figures 12 and 13);
- c) isolating from the reaction mixture the organic molecule and determining the structure or functional properties characterizing the organic molecule having the desired property (Abstract and Example 11-12 and Figures 12 and 13).

Iacobucci et al teach a method wherein the substrates are selected from amino acids (Abstract and Example 11-12).

Iacobucci et al inherently teach a method wherein the group of different substrates contain an unlimited number (including 1000) of different organic molecules (Column 4, line 66 to Column 5, line 16).

Iacobucci et al teach a method further comprising after step c), producing the organic molecule having the desired property (Example 11-12).

Iacobucci et al teach a method wherein the desired property is the ability to function as a drug (Column 19, lines 5-62).

Iacobucci et al teach a method wherein the substrates of the group of different substrates all share a common core structure (Column 7, lines 14-32).

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Iacobucci et al teach a method further comprising the step of using a selection method on the reaction mixture to produce a subset of organic molecules with a higher likelihood of producing the organic molecule having the desired property (Example 11-12).

Claim Rejections - 35 USC § 103

- 7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-12 and 16-24 are rejected under 35 U.S.C. 103 (a) over Civelli et al. (U.S. Patent 5,441,883) (August 15, 1995) in view of Furka et al. (International Journal of Peptide and Protein Research, (1991), Vol. 37, pages 487-493).

Civelli et al teach the method of claims 1-12 and 16-20 as described above.

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Civelli et al do not teach the step of dividing the reaction mixture of step (a) with different organic molecules into at least two subgroups, each containing less than all of the different organic molecules in the starting group.

Furka et al teach the step of dividing the reaction mixture of step (a) with different organic molecules into at least two subgroups, each containing less than all of the different organic molecules in the starting group (Page 487, Column 2, line 22 to Page 488, column 1, line 7, The principal of the method Section).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the step of dividing the reaction mixture of step (a) with different organic molecules into at least two subgroups, each containing less than all of the different organic molecules in the starting group of Furka et al. in the method for the production of an organic molecule having a desired property of Civelli et al. since Furka et al. state, "The efficiency of the method is remarkable (Page 492, Column 2, line 11)." By using these strong motivations as well as scientific reasoning, one ordinary practitioner would have combined and substituted the step of dividing the reaction mixture of step (a) with different organic molecules into at least two subgroups, each containing less than all of the different organic molecules in the starting group of Furka et al. in the method for the production of an organic molecule having a desired property of Civelli et al. to improve and control the efficiency of production of an organic molecule having a desired property. An ordinary practitioner would have been motivated to combine and substitute the step of dividing the reaction mixture of step

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(a) with different organic molecules into at least two subgroups, each containing less than all of the different organic molecules in the starting group of Furka et al. in the method for the production of an organic molecule having a desired property of Civelli et al., in order to achieve the express advantage, as noted by Furka et al, of the efficiency of a method which is remarkable.

9. Claims 29-35 are rejected under 35 U.S.C. 103 (a) over Shen et al. (U.S. Patent 3,932,498) (January 13, 1976) in view of Fodor et al. (Science, (15 February, 1991) (Vol. 251, pages 767-773).

Shen et al teach a method for the production and generating for characterization of an organic molecule having a desired property (Abstract), comprising the steps of:

- a) reacting a group of different substrates, the group comprising acids under suitable conditions with a dehydrating agent to yield a first reaction mixture (Column 5, lines 54-56 and column 8, Flowsheet);
- b) reacting the first reaction mixture with a reducing agent under suitable conditions to yield a second reaction mixture (Column 5, lines 56-58 and column 8, Flowsheet);
- c) reacting the first reaction mixture with an oxidizing agent under suitable conditions to yield a third reaction mixture (Column 5, lines 58-59 and column 8, Flowsheet);
- d) performing a condensation reaction under suitable conditions upon the third reaction mixture to yield a fourth reaction mixture (Column 5, lines 63-68 and column 8, Flowsheet);

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Shen et al do not teach a method of exposing an organic reaction mixture to light with a wavelength of about 220 nanometers to 600 nanometers, thereby producing one or more organic molecules different from the substrates and agents.

Fodor et al teach a method of exposing an organic reaction mixture to light with a wavelength of about 220 nanometers to 600 nanometers, thereby producing one or more organic molecules different from the substrates and agents (Abstract, Figures 1 and 3, and Page 767, Column 2, Light-directed peptide synthesis Section).

Shen et al do not teach a method of screening the exposed reaction mixture for the presence of the organic molecule and isolating the molecule having the desired property from the reaction mixture.

Fodor et al teach a method of screening the exposed reaction mixture for the presence of the organic molecule and isolating the molecule having the desired property from the reaction mixture (Figures 4-8).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the steps of exposing an organic reaction mixture to light with a wavelength of about 220 nanometers to 600 nanometers, thereby producing one or more organic molecules different from the substrates and agents of Fodor et al. in the method for the production of an organic molecule having a desired property of Shen et al. since Fodor et al. state, "High-density arrays formed by light-directed synthesis are potentially rich sources of chemical diversity for discovering new ligands that bind to biological receptors

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and for elucidating principles governing molecular interactions (Abstract, lines 9-13)." By using this strong motivation as well as scientific reasoning, one ordinary practitioner would have combined and substituted the steps of exposing an organic reaction mixture to light with a wavelength of about 220 nanometers to 600 nanometers, thereby producing one or more organic molecules different from the substrates and agents of Fodor et al. in the method for the production of an organic molecule having a desired property of Shen et al. to explore and discover the rich sources of chemical diversity. An ordinary practitioner would have been motivated to combine and substitute the steps of exposing an organic reaction mixture to light with a wavelength of about 220 nanometers to 600 nanometers, thereby producing one or more organic molecules different from the substrates and agents of Fodor et al. in the method for the production of an organic molecule having a desired property of Shen et al., in order to achieve the express advantage, as noted by Fodor et al, of the efficiency of a light-directed synthesis which is potentially rich sources of chemical diversity for discovering new ligands that bind to biological receptors and for elucidating principles governing molecular interactions.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this

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Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Chakrabarti,

Patent Examiner,

September 26, 2001

W. Gary Jones

Supervisory Patent Examiner Technology Center 1600